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May 2, 1990

Dr. Joshua Lederberg
President

Dear Dr. Lederberg:

Thank you kindly for your comments on our paper on the laser desorption of protein mixtures.

In answer to your questions:

- We would be delighted for you to leave a copy for David Baltimore.

- We have not yet performed detailed experiments on quantitation. However, our impression is that the technique is at least semi-quantitative because we have not observed any strong discrimination effects between different proteins or protein classes, (see for example Fig. 1 of our paper).

- So far, we have found that noncovalently bound subunits of proteins separate in the matrix or upon volatilization, even for chains that are expected to bond together rather strongly.

- Generally, there are two sources of peak broadening: (a) Peak heterogeneity in the protein samples e.g. on the attached sugar groups or elsewhere (we have found precious few proteins over mass 50,000 that are truly homogeneous) and (b) instrumental broadening arising primarily from events occurring during the desorption process.

- We have made a few measurements on DNA fragments that look quite promising and have, at least on paper (in a patent), devised a rapid (~10^6 bases/day) method for DNA sequencing.

- Hapten - Ig complexes intact? we need to do some experiments and perhaps come up with conditions that reduce the probability for dissociation.

- We are presently making plans (together with a commercial mass spectrometer manufacturer) to automate the instrument for use with HPLC and electrophoresis,

photoaffinity ligation

Sincerely,

Brian Chait